IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	09/989,674
Applicant	:	Gordon Woods
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TC/A.U.	:	1617
Examiner	:	Shaojla A. Jiang
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Director of the United States Patent
and Trademark Office
P.O. Box 1450
Alexandria, Virginia 22313-1450

DECLARATION PURSUANT TO 37 C.F.R. §1.132

I, Gordon L. Woods, declare that:

1. I am the same Gordon L. Woods identified as the applicant of the above-referenced patent application.

2. I received a B.S. degree from the University of Idaho in 1978 and a D.V.M. in 1978 from Colorado State University. I further received a M.S. in veterinary science in 1982 and a Ph.D. the following year from the University of Wisconsin. From 1983-1986 I was an Instructor and then an Assistant Professor at the New York State College of Veterinary Medicine in Ithaca, New York. From 1986-1988 I was an Associate Professor in the Department of Veterinary Clinical Medicine and surgery at Washington State University in Pullman, Washington. From 1988 to the present I have been a Professor at the University of Idaho, initially a Professor in Veterinary Science and currently a

Professor in Animal and Veterinary Science. For the past seven years, I also have been the President of CancEr2, Inc. A copy of my C.V. is attached hereto as Exhibit 1.

3. I have read and understand the rejections of the pending claims of the above-referenced application set forth in the outstanding Office Action of September 24, 2004. In that Action, the examiner rejected all of the pending claims under 35 U.S.C. §112, first paragraph, on the basis that the full scope of the claims is not enabled by the specification. More specifically, the examiner has asserted that although the specification is enabling for the specific low range of cadmium to be administered to a human by the particular route employed, the specification does not provide reasonable enablement for the full dose range of about 0.025 - 2 mg/day to be administered to a human by any route of administration in view of cadmium's known toxicity.

4. Cadmium has long been considered a nonessential element which can, indeed, be toxic to humans when administered in certain doses. As described in detail in my application, however, I have discovered that when administered in certain doses cadmium is not toxic, and, in fact, that humans can suffer from a cadmium deficiency, with adverse consequences, which can be treated through the administration of cadmium.

The examiner has asserted that the specification fails to provide sufficient information that would allow one of skill in the art to fully practice the invention without undue experimentation. The specification teaches daily dosage amounts and routes of administration and thus has provided guidance on how to use the invention. With regard to the examiner's concerns regarding toxicity, the application includes an example in which 1 mg of a cadmium salt was orally administered daily to a group of men for a six week period with no toxic effects. The application teaches the administration of cadmium in an oral dose as high as 2 mg per day, and a further experiment detailed below illustrates that this dose can be administered safely with no toxic effects to the patient.

5. A daily oral dose of 2 mg of cadmium sulfate was administered to a healthy human male over a nine week period. The cadmium sulfate was administered every morning, one hour prior to any food intake. Blood and urine samples were collected from the man one day prior to the beginning of treatment (considered day 1 of the study) and then on days 20, 34, 48, 62 and 73. The cadmium sulfate was administered daily on days 2 - 64 of the study period. In order to standardize body chemicals prior to sample collection, the man food fasted for 24 hours each day that the blood and urine were collected, beginning at 6:00

p.m. the evening before the sample collections and continuing until 6:00 p.m. the evening of the collection day. Samples were collected between 10:00 a.m. and 3:00 p.m. Two liters of bottled water were provided to the man to drink freely throughout the sample collection day. Complete urinalysis, comprehensive metabolic, urine protein and hemogram tests were preformed on the blood and urine samples.

No evidence of toxicity was detected throughout the nine week cadmium treatment protocol. Protein in the urine is a symptom of cadmium toxicity. Trace protein was detected in the man's urine on days 20 and 34 of the protocol, but no protein was detected on days 48, 62 and 73. As a result, the trace protein detected on days 20 and 34 was interpreted as incidental and not to have been caused by the cadmium administration.

This protocol illustrates that 2 mg of a cadmium salt can be safely administered for an extended period to humans.

6. In addition to the claims of my application directed to the oral administration of cadmium in a dosage range of about 0.5 to about 2 mg per day, there also are claims directed to the parenteral administration of a cadmium salt in a dosage range of about 0.025 to about 0.1 mg per day. When cadmium is administered orally, approximately 95% of the cadmium will pass through the gastro-intestinal tract and not be absorbed into the

blood, tissue or other organs. *WHO Food Additives Series #24*, p.166 (1989), citing Kitamura, 1972; Rahola et al., 1972; Yamagata et al., 1974; Flanagan et al., 1978; and Shaikh and Smith, 1980. Thus, only about 5% of the cadmium administered orally is available in the body as a therapeutic agent. In contrast, when cadmium is administered parenterally, it is systemically absorbed. Accordingly, only about 5% of the amount administered orally is necessary for parenteral administration to achieve comparable results. Thus, as suitable oral dosages are within the range of about 0.5 mg to about 2 mg per day, suitable parenteral doses are within the range of about 0.025 to about 0.1 mg per day.

7. Further evidence that cadmium administration at the doses provided in my application are not toxic and will serve to treat a cadmium deficiency can be extrapolated from "Toxicological Evaluation of Certain Food Additives and Contaminants," prepared by the 33rd Meeting of the JOINT FAO/WHO Expert Committee on Food Additives and published in 1989 in the *WHO Food Additives Series #24*, pp 182-219. A copy of this paper is attached hereto as Exhibit 2.

This paper reports on toxicity studies in which cadmium salts were orally administered to male rhesus monkeys in varying dosages and over different periods of time. Rhesus monkeys are a

good model for humans because humans and rhesus monkeys metabolize cadmium similarly. Nomiyama et al., *Environ. Health Perspect.* 28:223-243 (1979). In reviewing the FAO/WHO report, I have assumed an average weight for the monkeys of 12.5 kg. If one also assumes an average weight for human males of 70 kg, the per weight conversion factor is 5.6 to determine the comparable amounts of cadmium that could be administered to humans to achieve similar results. In the first study reported, each monkey was given 0.1, 0.3, 3.0 or 30.0 mg of cadmium salt per day (100 g of food containing 1, 3, 30 or 300 mg/kg, respectively); the equivalent dose of cadmium per human would have been 0.56, 1.68, 16.8 and 168 mg cadmium/day. The study continued for 24 weeks. No toxicity was shown for monkeys who received the lowest dose, equivalent to humans receiving 0.56 mg/day. Toxicity was shown in monkeys receiving the highest dose, which significantly exceeds the maximum dose taught in my patent application; no report was provided regarding the intermediate doses.

In a second study, for one month groups of monkeys received 0, 0.3, 1.0, 3.0 or 10.0 mg cadmium/day (100 g of food containing 0, 3, 10, 30 or 100 mg/kg, respectively), equivalent to adult humans receiving 0, 1.68, 5.6, 16.8 or 56 mg cadmium/day, then for 13 months were administered 0, 0.45, 1.5, 4.5 or 15.0 mg cadmium/day, respectively, equivalent to 0, 2.52, 8.4, 25.2 or

84.0 mg cadmium/day for adult humans. For the following 16 months, the monkeys received 0, 0.6, 2.0, 6.0 or 20.0 mg cadmium/day, respectively, equivalent to 0, 3.36, 11.2, 33.6 or 112.0 mg cadmium/day for adult humans. The paper reports that no adverse effects were recorded for the monkeys who received 3 mg/kg food/day (the human equivalent of 1.68 mg/day for one month, 2.52. mg/day for the next 13 months and 3.36 mg/day for the following 16 month) and in the 10 mg/kg food/day group (the human equivalent of 5.6 mg/day for one month, 8.4 mg/day for the next 13 months and 11.2 mg/day for the next 16 months) "slight pathological changes were observed in the tubular epithelium during the 101st week but no other adverse effect were noted." These results indicate that the maximum doses advocated in my application would be safe and non-toxic.

In a third study, rhesus monkeys received a cadmium salt at a level of 3 mg/kg food (the human equivalent of 1.68 mg/day) for one year, with some receiving a dose of up to 30 mg/kg food (the human equivalent of 16.8 mg/day) for a further two years. The authors report that after 3 years, no proteinuria or abnormalities in creatinine clearance were noted. Again, these results indicate that the maximum doses set forth in my application for human administration are safe and non-toxic.

The paper further reports the results of a long-term study that continued for up to 9 years, in which rhesus monkeys received 200g of feed/day to which were added a cadmium salt at a concentration of 0, 3, 10 , 30 or 100 mg. The monkeys thus received 0, 0.6, 2.0, 6.0 or 20.0 mg cadmium/day, respectively, which if administered to humans would be 0, 3.36, 11.2, 33.6 or 112 mg/day, respectively. The authors report that no renal function abnormality was seen in the 3 or 10 mg/kg dose groups (3.36 mg/day/human equivalent or 11.2 mg/day/human equivalent). No pathological changes in the kidneys were noted for the 3 mg/kg group; mild lesions were observed in the 10 mg/kg group. These results also indicate that the maximum dose recommended in my application is nontoxic in humans.

8. The results provided in the FAO/WHO study and from my own studies indicate that the cadmium doses for humans set forth in my application are non-toxic and can be administered safely.

9. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the

United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

_____
Gordon L. Woods

_____
Date

Exhibit 1

CURRICULUM VITAE

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Ph.D., 1982-1983, University of Wisconsin
M.S., 1980-1982, University of Wisconsin
Residency in Large Animal Reproduction, 1979-1980, University of Pennsylvania
D.V.M., 1974-1978, Colorado State University
B.S., 1971-1974, University of Idaho
1970-1971, Ricks College, Rexburg, Idaho

BOARD CERTIFICATION:

Diplomate, American College of Theriogenologists, 1983

EXPERIENCE:

1998-present, President, CancEr2 Inc.
1988-present, Professor, Department of Animal and Veterinary Science, University of Idaho, Moscow, Idaho
1986-1988, Associate Professor, Department of Veterinary Clinical Medicine and Surgery, Washington State University, Pullman, Washington
1984-1986, Assistant Professor, Section of Reproduction, New York State College of Veterinary Medicine, Ithaca, New York
1983-1984, Instructor, Section of Reproduction, New York State College of Veterinary Medicine, Ithaca, New York
1980-1983, Research Assistant in Dr. O.J. Ginther's Reproduction Laboratory, University of Wisconsin, Madison, Wisconsin
1979-1980, Residency in Large Animal Reproduction with Dr. Robert M. Kenney, University of Pennsylvania, Kennett Square, Pennsylvania
1978-1979, Practitioner in a seven-person mixed practice, Lewiston Veterinary Clinic, Lewiston, Idaho

ADMINISTRATION:

1986-present, Originator and Director of the Northwest Equine Reproduction Laboratory, University of Idaho, Moscow, Idaho
1988-1990, Head, Department of Veterinary Science, University of Idaho, Moscow, Idaho; Director of the Idaho portion of the Washington/Oregon/Idaho Regional Program in Veterinary Medicine
1984-1986, Originator and Director of Cornell's Laboratory of Equine Embryo Biology, New York State College of Veterinary Medicine, Ithaca, New York

AWARDS:

Idaho Veterinarian of the Year (Idaho Veterinary Medical Association, 2004)
George Oakshott Award (North Idaho Veterinary Medical Association, 2002)
Gamma Sigma Delta Research Award (University of Idaho, 1997)
Huesped de Honor (Universidad Nacional de Rio Cuarto, 1994)
Norden Distinguished Teacher Award (Washington State University, 1988)
Burr A. Beach Award (University of Wisconsin, 1983)

GRADUATE STUDENTS:

Major Advisor:

Tonia Gable, B.S., completed her M.S. at the University of Idaho in 1999 (Thesis: Increased Cumulus Expansion of Equine Cumulus Oocyte Complexes is Correlated to Increased Nuclear Development and Increased Culture Time of Equine Cumulus Oocyte Complexes Increases Nuclear Development). Tonia is a veterinary practitioner in Idaho.

Marcelo Miragaya, D.V.M., completed his M.S. at the University of Idaho in 1997 (Thesis: Uterine and Oviductal Inflammation and Fertilization Rates of Mares with Intrauterine Luminal Fluid or 1% Glycogen Treatment). He completed his Ph.D. in 1999 (Dissertation: Cumulus Cell, Ooplasmic and Nuclear Morphology of Peri-ovulatory Equine Oocytes and Ova by Confocal Laser Scanning Microscopy.) Marcelo is a faculty member at the University of Buenos Aires.

Larry Olsen, D.V.M., M.S. completed his Ph.D. at the University of Idaho in 1999 (Dissertation: Hoechst 33342-Preloaded Jack Sperm Penetrate Mare Cumulus Oocyte Complexes (COCs) and Hoechst 33342-Preloaded Bull Sperm Penetrate Cow COCs; Caffeine Increases Jack Sperm Hyperactivation But Not Sperm Penetration of Mare COCs; and Increased Concentration of Jack Sperm At Collection Appears to Increase Penetration of Mare COCs). Larry is working in Puerto Rico.

Jose Javier Aguilar, D.V.M., completed his M.S. at the University of Idaho in

1996 (Thesis: Living Fibroblast Cells in the Oviductal Masses of Mares). He completed his Ph.D. at the University of Idaho in 1998 (Dissertation: Follicular Fluid Induced Nuclear Maturation and Cumulus Expansion of Equine Cumulus Oocyte Complexes, Follicular Shells Increased Maturation of Denuded Oocytes, and Additional Culture in Dmem-Ham's F12 Increased Cumulus Expansion). Javier is a faculty member at the University of Edinburgh.

Anne B. Lichtenwalner, D.V.M., completed her Ph.D. at the University of Idaho in 1995 (Dissertation: Mechanism of Oviductal Transport in the Mare and Reproductive Behavior, Ejaculatory Pattern and Seminal Parameters in the Male Llama. Uterine Transport and Maternal Recognition of Pregnancy in the Mare). Anne is a former faculty member at the University of Washington.

James A. Weber completed his M.S. at the University of Idaho in 1989 (Thesis: Ultrasonographic Studies of Bull and Stallion Accessory Sex Glands). He completed his Ph.D. at the University of Idaho in 1992 (Dissertation: Embryonic Prostaglandin E_2 Secretion and the Initiation of Selective Oviductal Transport in the Mare). He completed his D.V.M. at Washington State University in 1994. Jim is a tenured faculty member at the University of Maine.

Dirk K. Vanderwall, D.V.M., completed his Ph.D. at the University of Idaho In 1992 (Dissertation: Prostaglandin E_2 Secretion by the Equine Embryo and Its Role in Uterine Transport and Maternal Recognition of Pregnancy in the Mare). He is board certified in the American College of Theriogenologists. Dirk is a faculty member at the University of Idaho.

Douglas A. Freeman, D.V.M., completed his Ph.D. at the University of Idaho In 1991 (Dissertation: Studies in Selective Oviductal Transport in the Mare). He is board certified in the American College of Theriogenologists. Doug is a faculty member and Department Head for the Department of Veterinary and Microbiological Sciences at the University of North Dakota.

Barry A. Ball, D.V.M., completed his Ph.D. at Cornell University in 1987 and received tenure at Cornell University. (Dissertation: Studies on Embryonic Loss in Young, Normal Mares and Aged, Subfertile Mares). During his graduate training, Barry became board certified in the American College of Theriogenologists. Barry is the John Hughes Distinguished Professor at the University of California, Davis.

Committee Member:

Jessica Williams, Ph.D. candidate, University of Idaho
Leslie Hartt, M.S., University of Idaho, 2003
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PUBLICATIONS:

Refereed Journal Articles:

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WHO FOOD ADDITIVES SERIES: 24

Toxicological evaluation of certain food additives and contaminants
Prepared by THE 33rd MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

IPSC International Programme on Chemical Safety

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Monkeys
Ten male rhesus monkeys were divided into four groups of 2, 2, 3 and 3 and were fed daily 100 g food containing 1, 3, 30 and 300 mg Cd/kg respectively. Urine was collected every 2 weeks and blood samples every 4 weeks. One monkey from each of the two top treatment groups was sacrificed at week 24 for pathological examination and determination of tissue cadmium levels.

The lowest dose group did not show any effect of treatment over a period of 55 weeks. The 30 mg/kg group showed no significant changes for up to 24 weeks although urine levels were up to 18 microg Cd/L and, in the animal sacrificed at this time, the renal cortex cadmium concentration was 300 mg/kg. In this group plasma urea nitrogen and urine protein increased after 30 and 36 weeks. After 55 weeks, qualitative tests were negative for low molecular weight proteinuria and glycosuria; blood analyses and liver and kidney function tests were essentially normal although the cadmium concentrations in the renal cortex of the two monkeys were 460 and 730 mg/kg and those in the liver were 110 and 160 mg/kg, respectively.

In the highest exposure group, renal dysfunction was observed as total proteinuria, increased excretion of beta-2-microglobulin and retinol binding protein, glucosuria, aminoaciduria, decreased creatinine clearance and decreased tubular reabsorption of phosphate. Cadmium concentration in the renal cortex and liver of the two monkeys was 350 and 580 mg/kg, and 410 and 630 mg/kg, respectively. The critical cadmium concentration in the renal cortex was estimated as 380 mg/kg for low molecular weight proteinuria and 470 mg/kg for proteinuria, glucosuria and aminoaciduria. The apparent biological half-life of cadmium at autopsy was calculated to be 22.4, 5.2, 6.4 and 0.66 years for the 0, 3, 30 and 300 mg/kg groups, respectively (Nomiyama et al., 1979).

In a second experiment, 35 rhesus monkeys were divided into five groups and each group were fed pelleted food containing 0, 3, 10, 30 or 100 mg/g respectively at a daily dose of 100 g for one month, 150 g for the next 13 months and 200 g for the following 16 months. Urine and blood samples were examined every 3rd and 6th week respectively. One animal from each group was sacrificed for tissue cadmium determination and pathological examination after 60 and 101 weeks; additional animals were sacrificed from the top dose group after 39 and 50 weeks, and from the 30 mg/kg group after 72 weeks and similarly examined.

No adverse effects were recorded in the 3 mg/kg group. In the 10 mg/kg group, slight pathological changes were observed in the tubular epithelium during the 101st week but no other adverse effects were noted. In the 30 ppm group, slight proteinuria (described as "negligeable") was detected after 58 weeks but no pathological changes were seen and cadmium concentration in the renal cortex after 60 weeks was 809 mg/kg. During the 101st, week slight pathological changes were observed in the tubular epithelium in this dose group when the renal cortex cadmium concentration was 844 mg/kg. It was concluded that the critical concentration for proteinuria was 780 mg/kg for proteinuria and in excess of 840 mg/kg for histopathological changes.

In the 100 mg/kg dose group, slight proteinuria, aminoaciduria and beta-2-microglobulinuria occurred after the 39th-42nd week when the cadmium concentration in the renal cortex was 635mg/kg. Subsequently, marked proteinuria, aminoaciduria and decreases in renal function were observed during the 48th-54th week when the cadmium concentration in the cortex was 612 mg/kg. Renal function further deteriorated with time of exposure and, at termination, marked tubular pathology was evident. After 101 weeks the cadmium concentration in the renal cortex was 560 mg/kg.

These results were taken to indicate that the critical concentration for proteinuria, aminoaciduria, beta-2-microglobulinuria, glycosuria, renal dysfunction and pathological changes were all approximately 635 mg/kg. However, other changes (elevated plasma enzymes and anaemia) were detected after 6 and 543 weeks, respectively, in the 100 mg/kg dose group (Nomiyama et al., 1982a).

Forty male and female rhesus monkeys were divided into eight groups (4-8 per group). Half were given a diet containing cadmium chloride at a level of 3 mg/kg for one year and ten at a level of up to 30 mg/kg for a further 2 years. The other half were given no additional cadmium above normal pelleted food. Some animals received diets low in calcium and /or vitamin D. No proteinuria was noted after 3 years and no abnormalities in creatinine clearance of phenolsulphophthalein test. Cadmium concentrations in the renal cortex of monkeys given cadmium and maintained on a low calcium and vitamin D deficient diet were between 611 and 1017 mg/kg after the third year of the experiment. Biopsy specimens of renal cortex from 2 monkeys given cadmium in an adequate diet contained 624 and 1255 mg/kg respectively at the 50th month (Tertiary Monkey Experiment Team, 1983).

Long term studies

Monkeys

In a long-term study thirty seven male rhesus monkeys, age about 3 years, were divided into five groups and given daily 200 g solid feed containing added cadmium chloride at concentrations of 0, 3, 10, 30 or 100 mg Cd/kg respectively; the basal diet contained the minimum requirement of zinc of 6 mg/day (30 mg/kg) in order to avoid the protective effect of excess zinc and was found to contain 0.27 mg Cd/kg. The exposure was

continued for up to 9 years. Urine and blood specimens were collected at three and six week intervals respectively and the animals were examined for haemopoietic, circulatory, liver and renal functions, calcium and phosphate metabolism and blood and urine metal levels. Lumbar X-ray examinations were carried out at 12 week intervals and animals were sacrificed at regular intervals for histopathological examination and determination of organ metal concentrations.

Dose related decreases in weight and body length were recorded in the groups given 10 mg Cd/kg diet or more. Over 50% of the 100 mg/kg showed decreased erythrocyte counts after 120 weeks and a similar effect occurred after 240 weeks and 360 weeks in the 30 mg/kg group and 10 mg/kg groups respectively. The anaemia was not accompanied by an increase in reticulocytes. The highest dose group had a higher blood pressure than other groups during the first 18 months but the age related increase in the controls was not seen in the test animals. No change was seen in ECG or pulse rate.

The 100 mg/kg group displayed glucosuria, proteinuria after 48 weeks and plasma creatinine and phosphorous clearance values were elevated. Plasma uric acid was elevated at 84 weeks and the frequency of aminoaciduria increased from 91 weeks. Urine volume was increased from 101 weeks and beta-2-micoglobulin began to rise from 138 weeks and exceeded 2 mg/L at 172 weeks.

The 30 mg/kg group showed an increase in plasma uric acid at 300 weeks and from 306 weeks there was an increase in urine amino acids and plasma creatinine. Beta-2-microglobulinuria was noted at 311 weeks and exceeded 2 mg/L at 426 weeks; total proteinuria was observed at 384 weeks.

The onset of beta-2-microglobulinuria was later than other clinical indications of renal dysfunction in the 100 mg/kg dose group but these indicators coincided in the 30 mg/kg group. Despite the early clinical signs at 48 weeks in the top dose group, there was no marked aggravation of the condition over the following eight years and no case of renal failure developed.

No abnormality of renal function was seen in the 3 or 10 mg/kg dose groups.

In the highest dose group, elevated plasma GOT and GPT were detected from 6 weeks and increased LDH and deceased plama A/G ratios from 18 weeks. No other indications of liver dysfunction were seen in any dose group. No radiological or clinical biochemical change in bone mineral metabolism were seen and serum vitamin D levels and metabolism in the kidney appeared normal (see also Short-term Studies, Tertiary Monkey Experiment Team, 1983).

Histologically, dose dependant pathological changes were seen in the kidneys of the 10, 30, and 100 mg/kg groups but the lesions were only classified as mild to moderate. Even at the top two dose levels, the changes were not particularly progressive and only mild renal cortical fibrosis was evident at completion of the 9 year experiment. No osteomalacia or osteoporosis was observed in the femur.

Cadmium excretion in the urine showed an exponential relationship to dose and duration of exposure and did not increase following signs of renal dysfunction. Concentration in the renal cortex increased to a maximum of 635 mg/kg at 39 weeks in the 100 mg/kg group, 1170 mg/kg at 257 weeks in the 30 mg/kg groups and 1070 mg/kg at 216 weeks in the 10 mg/kg group, after which there was a decrease irrespective of the absence or presence of renal dysfunction. Cadmium levels in the liver of the top dose group reached a maximum of 1040 mg/kg after 101 weeks but in all other groups it continued to rise until completion of the experiment when the levels were 106, 430 and 1400 mg/kg in the 3, 10 and 30 mg/kg groups, respectively.

Administration of cadmium caused a dose-dependent increase in copper and zinc concentrations in blood, plasma, renal cortex and liver. Organ levels of copper and zinc fell and urinary excretion of these metals increased following the onset of renal dysfunction.

It was estimated that the critical concentration of cadmium in the renal cortex was 635 mg/kg in the 100 mg/kg group and 1170 mg/kg in the 30 mg/kg group (Nomiyama et al., 1987).

In a long-term study to investigate whether any difference in toxicity could be detected between cadmium in contaminated rice and inorganic cadmium, crab-eating monkeys were given diets containing rice to a level of 80 microg Cd/day, or cadmium chloride to a level of 190 g Cd/day. Two animals on standard diets served as controls. The experiment was conducted over a period of 6 years. Effects due to treatment included high urinary cadmium (occasionally exceeding 10 microg/L) but no changes could be detected in urinary beta-2-microgloculin, renal or hepatic function nor any other haematological or clinical biochemical index. Cadmium concentrations in the renal cortex and liver increased proportionally to the dose level and duration of exposure and renal cortex levels reached a maximal of 570 mg/kg after CdCl2 and 300 mg/kg after contaminated rice (Nomiyama & Nomiyama, 1988).

In the absence of significant treatment-related differences in organ function and pathology, and in the light of the different doses used in rice and as inorganic cadmium, it is not possible to reach conclusions about the relative toxicity of inorganic cadmium and that in contaminated rice.

FDA scales risk-per-unit dose according to a simple dose/ body-weight rule (page 301, third Edition "Principles and Methods of toxicology", Editor- A. Wallace Hayes, Raven Press).

BBC - Science & Nature - Wildfacts - **Rhesus monkey**
... Life span **Rhesus monkeys** live for about four years in the wild, although in ... Statistics **Body** length: 45-64cm, Tail length: 19-32cm, ***Weight: Males 6.5-12kg*** ...
www.bbc.co.uk/nature/wildfacts/factfiles/211.shtml - 29k - Cached - Similar pages